DETAILED ACTION

Status of the Claims

Claims 1-7 are pending.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Information Disclosure Statement

Receipt of the Information Disclosure Statement filed on 08/15/08 and 04/25/11 is acknowledged and has been entered into the file. Signed copies of each 1449 is attached herewith.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 7 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 provides for the use of a compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3 and 5-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since

the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, the claims recite the broad recitation of specific acid addition salts, and the claim also recites "such as (D)(-) tartrate salt or (L)(+) tartrate salt etc., which is the narrower statement of the range/limitation. The same rejection applies to the use of the “particularly a D-malate salt” in claim 5 and “especially” in claim 7 respectively.

Claim Rejections - 35 U.S.C. § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

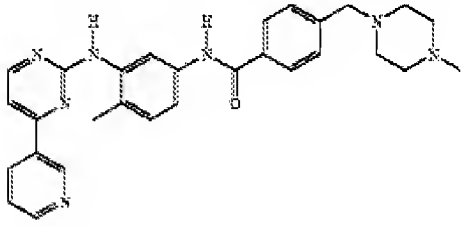
Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmermann et al., (WO 99/03854) in view of Ekwuribe et al., (U.S.Patent number 6,479,692)('692').

Applicants claim various salts of 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl[-benzamide structural formula



The claims are drawn to salts such (D)(-) tartrate salt, pamoate salt, a formate salt etc.

Claims 5 and 6 are drawn to pharmaceutical compositions containing the claimed salts.

Zimmermann et al., disclose a crystal methanesulfonic acid addition salt structurally similar to the claimed salts. See the entire reference especially page 3, formula (I), and page 4 formula (II). Note Examples 4 and 6 teaches composition containing the claimed compounds is known in the art.

Additionally, page 9, third paragraph teaches that the acid addition salt is used as an anti-tumor agent, which is the utility claimed herein. Also see pages 16 and 17, starting with the last paragraph of page 16 to the first paragraph of page 17.

The instant claims differ from Zimmermann in that the reference discloses a crystalline methanesulfonic acid addition salt form of the compound whereas the instant claims are drawn to other non-crystalline salt forms. However, changing the form, purity or other characteristics of an old compound is considered *prima facie obvious* and does not render the novel form patentable where the difference in form, purity or characteristics is inherent in the prior art. *See In re Best,* 562 F 2d. 1252, 1254, 195 U.S.P.Q. 430, 433 (CCPA 1977)

Moreover, Ekwuribe et al. discloses that salts such as tartrate, HCl salts etc., are salts that retain the desired biological activity of the parent compounds. See column 11, lines 15-30. Thus, there is ample motivation for one of ordinary skill in the art to modify the prior art compounds to arrive at the instantly claimed salts because Ekwuribe et al., discloses that pharmaceutically acceptable salts are salts that retain the desired biological activity of the parent compounds and do not impart undesired toxicological effects. Thus, the selection of the specific claimed salts is not a patentable distinction but, rather a matter of choice.

The motivation to prepare these compounds derives from the fact that the resulting salt would reasonably be expected to be useful for treating leukemia and other tumors since Ekwuribe et al., discloses that pharmaceutically acceptable salts retain the desired biological activity of the parent compounds and do not impart undesired

toxicological effects. Therefore, the instantly claimed salt would have been suggested to one of ordinary skill in the art absent a showing of unobvious results and/or properties.

Claim Rejections - 35 U.S.C. § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

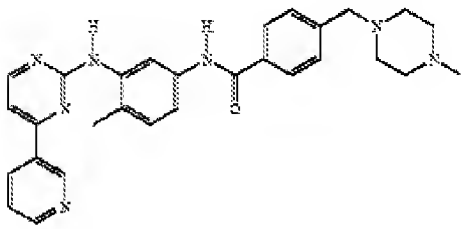
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmermann et al., (WO 99/03854) in view of Ekwuribe et al., (U.S.Patent number 6,479,692)('692').

Applicants claim the treatment of a tumor disease such as leukemia by administering various acid addition salts containing 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl[-benzamide structural formula



The various salts such (D)(-) tartrate salt, pamoate salt, a formate salt etc., are the salt of choice.
Zimmermann et al., disclose methanesulfonic acid addition salt structurally similar to the claimed salts which are used as anti-tumor agent, which is the method claimed herein. See pages 9, the third paragraph; 16 and 17, starting with the last paragraph of page 16 to the first paragraph of page 17.

The instant claim differs from Zimmermann in that the reference discloses the use of a crystalline methanesulfonic acid addition salt form of the compound whereas the instant claim is drawn to the use of non-crystalline salt forms. However, changing the form, purity or other characteristics of an old compound is considered *prima facie obvious* and does not render the novel form patentable where the difference in form, purity or characteristics is inherent in the prior art. *See In re Best,* 562 F 2d. 1252, 1254, 195 U.S.P.Q. 430, 433 (CCPA 1977)

Moreover, Ekwuribe et al. discloses that salts such as tartrate, HCl salts etc., are known in the art and such salts retain the desired biological activity of the parent compounds. See column 11, lines 15-30. Thus, there is ample motivation for one of ordinary skill in the art to modify the prior art compounds to arrive at the instantly claimed salts to treat leukemia because Ekwuribe et al., discloses that pharmaceutically acceptable salts are salts that retain the desired biological activity of the parent compounds and do not impart undesired toxicological effects. Thus, the selection of the specific claimed salts to treat leukemia is not a patentable distinction but, rather a matter of choice.

The motivation to employ the use of these compounds derives from the fact that the resulting salt would reasonably be expected to be useful for treating leukemia and other tumors since Ekwuribe et al., discloses that pharmaceutically acceptable salts retain the desired biological activity of the parent compounds and do not impart undesired toxicological effects. Therefore, the instantly claimed treatment would have been suggested to one of ordinary skill in the art absent a showing of unobvious results and/or properties.

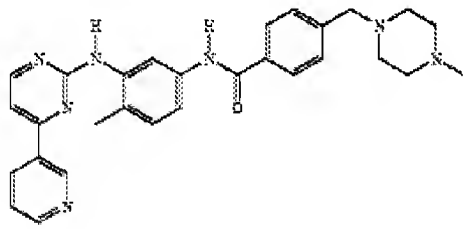
Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 7,893,076 in view of Ekwuribe et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed compounds and composition and those of Patent No. 7,893,076 contain members of the Markush groups that overlap substantially. Specifically, the current core of the pending claims is drawn to specific salts of  (imatinib). Also note that Ekwuribe teaches that pharmaceutically acceptable salts retain the desired biological activity of the parent compounds and do not impart undesired toxicological effects. The difference between the instant application and the patent is the slight differences in Markush members for the salts representing the variables.

The overlap of the variables suggests the instant compounds and renders same prima facie obvious.

The motivation to prepare these compounds derives from the fact that structurally similar compounds would possess virtually the same or similar properties. Hence, one of ordinary skill in the art would be motivated to prepare the instant compounds and compositions with a reasonable expectation that the resulting compounds would be useful for the pharmaceutical industry.

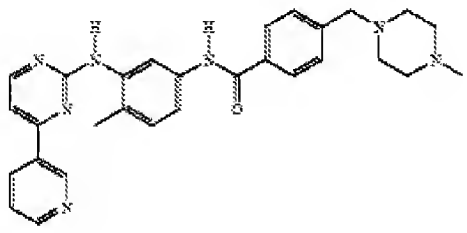
Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 7 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 70-71 of U.S. Patent Application No. 13/006,505 in view of Ekwuribe et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the use of the instantly claimed compounds and composition and those of '505' contain members of the Markush

groups that overlap substantially. Specifically, the current core of the pending claims is drawn to specific salts of  (imatinib). Also note that Ekwuribe teaches that pharmaceutically acceptable salts retain the desired biological activity of the parent compounds and do not impart undesired toxicological effects. The difference between the instant application and '505' is the use of the salts representing the variable salts for treating leukemia.

The use of the variable art recognized pharmaceutical salts of the same compound (imatinib) suggests the instantly claimed method and renders same *prima facie* obvious.

See MPEP 2112, which states, "Something which is old does not become patentable upon the discovery of a new property. The claiming of a new use, new function or unknown property, which is inherently present in the prior art, does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 U.S.P.Q. 430, 433 (CCPA 1977)."

The motivation to use these compounds derives from the fact that structurally similar compounds would possess virtually the same or similar properties. Hence, one of ordinary skill in the art would be motivated to prepare and use the instant compounds and compositions with a reasonable expectation that the resulting compounds would be useful in the pharmaceutical industry.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to EBENEZER O. SACKEY whose telephone number is (571)272-0704. The examiner can normally be reached on 7.30-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/EBENEZER O SACKEY/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, AU 1624